CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-086

CORRESPONDENCE

Taylor
Pharmaceuticals an Akorn Co.

• generics • injectables • ophthalmics • contract services

NEW CORRESP

FAX/NC

February 25, 1998

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: GENERAL CORRESPONDENCE
ANDA 75-086
Diltiazem Hydrochloride Injection
5 mL and 10 mL fill sizes

Dear Sir:

Reference is made to our teleconference on Tuesday afternoon, February 24, 1998 between Adolph Vezza and Charlie Hoppes (FDA Division of Labeling Support) and Jim Baumann, Rick Taylor, and Lou Fraser (Taylor Pharmaceuticals). The teleconference was held in regard to Taylor's request for clarification on comments provided in the FDA Fax, dated February 24, 1998. This FAX was FDA's response to Taylor's recent submission (Minor Amendment to ANDA 75-086) of January 30, 1998, which had addressed certain microbiology and labeling deficiencies in ANDA 75-086.

In addition to clarification of certain items in the FDA FAX, Taylor had requested FDA, during the teleconference, to consider its proposal to approve ANDA 75-086 with the current labeling based on the following commitment(s):

1. Taylor ***will revise*** the container and carton labeling in accordance with the requests made in the FDA FAX of February 24, 1998;

2. Taylor will provide the revised labeling ***(post-approval)*** as a "Supplement - Changes Being Effected" to the file for ANDA 75-086;

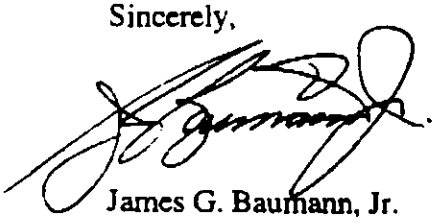
3. The requirements for revised labeling will be used to label the finished drug product ***prior to its release*** to the market place.

FDA indicated that they would take Taylor's *verbally proposed commitments* under consideration and later discussed same with Robert West (FDA Division of Labeling Support). As a result of this discussion, Taylor was notified by Adolph Vezza (FDA Labeling Division) on Wednesday morning, February 25, 1998 that FDA concurred with

Taylor's commitments regarding approval of ANDA 75-086 and the corresponding revisions to the container and carton labeling. Taylor will proceed accordingly to revise its labeling and provide same as a post-approval Supplement - Changes Being Effected to the file for ANDA 75-086.

Should additional information and/or clarification be required, please contact me at (217) 423-9715, or FAX (217) 423-5206.

Sincerely,



James G. Baumann, Jr.
Manager, Regulatory Submissions

Taylor Pharmaceuticals *an Akorn Co.*

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January 30, 1998

NDA ORIG AMENDMENT
AM
2/5/98
AM noted. To Micro for review, then labeling, then Chemistry

Office of Generic Drugs, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: MINOR AMENDMENT TO ANDA 75-086
Diltiazem Hydrochloride Injection, 5 mg/mL
5 mL and 10 mL Vials

Dear Sir/Madam:

Taylor Pharmaceuticals (an Akorn Company), a manufacturer, marketer, and distributor of ophthalmic and injectable drug products hereby submits this Minor Amendment to our ANDA 75-086 for Diltiazem Hydrochloride Injection, 5 mg/mL, an injectable drug intended for use in adult patients for the temporary control of rapid ventricular rate in atrial fibrillation or atrial flutter and for the rapid conversion of paroxysmal supraventricular tachycardias (PSVT) in sinus rhythm. The reference listed drug (RLD) is Cardizem® Injectable, the subject of NDA 20-027, which is held by Marion Merrell Dow and was approved on October 24, 1991.

This amendment is in response to the FDA Deficiency Letter (Facsimile), dated December 30, 1997, listing *minor deficiencies (Microbiology/Labeling)* regarding ANDA 75-086 and requesting Taylor to provide a complete response to these deficiencies as a "Minor Amendment".

A listing of the contents of this amendment is provided for convenience of review.

Taylor is filing an archival copy consisting of one volume (in blue folder) of this amendment and a technical review copy (in red folder) which is identical to the archival copy. An additional certified field copy (in maroon folder) was sent to the Chicago District Office.

In accordance with 21 CFR § 314.96 (b), and by reference 314.60 (c), Taylor Pharmaceuticals certifies that a true copy of this Minor Amendment to ANDA 75-086 for Diltiazem Hydrochloride Injection, 5 mg/mL, has been provided to the FDA Chicago District Office. A copy of this certification with an original signature is provided with this amendment as **Attachment M.**

RECEIVED
FEB 0 3 1998

Madam 2/4/98

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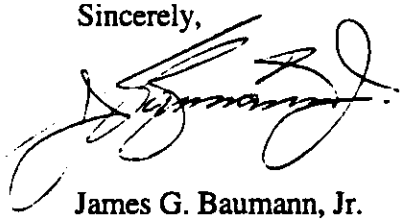
Should additional information be required regarding this amendment, please feel free to contact me at (217) 423-9715 or FAX (217) 428-8514.

Sincerely,



James G. Baumann, Jr.
Manager, Regulatory Submissions

Taylor Pharmaceuticals *an Akorn Co.*

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November 14, 1997

Office of Generic Drugs, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RECEIVED
NOV 17 1997
GENERIC DRUGS

RE: FACSIMILE AMENDMENT TO ANDA 75-086
Diltiazem Hydrochloride Injection, 5 mg/mL
5 mL and 10 mL Vials

Dear Sir/Madam:

Taylor Pharmaceuticals (an Akorn Company), a manufacturer, marketer, and distributor of ophthalmic and injectable drug products hereby submits this Facsimile Amendment to our Abbreviated New Drug Application for Diltiazem Hydrochloride Injection, 5 mg/mL, an injectable drug intended for use in adult patients for the temporary control of rapid ventricular rate in atrial fibrillation or atrial flutter and for the rapid conversion of paroxysmal supraventricular tachycardias (PSVT) in sinus rhythm. The reference listed drug (RLD) is Cardizem® Injectable, the subject of NDA 20-027, which is held by Marion Merrell Dow and was approved on October 24, 1991.

This amendment is in response to the FDA Deficiency Letter (Facsimile), dated October 17, 1997, listing minor deficiencies and/or comments regarding ANDA 75-086 and requesting Taylor to provide a complete response to these deficiencies as a "Facsimile Amendment".

For ease of reference, this amendment is numbered sequentially in the lower right corner so that both the text and attachments bear consecutive numbers. A table of contents is provided for additional convenience of review.

Taylor is filing an archival copy consisting of one volume (in blue folder) of this amendment and a technical review copy (in red folder) which is identical to the archival copy. An additional certified field copy (in maroon folder) was sent to the Chicago District Office.

In accordance with 21 CFR § 314.96 (b), and by reference 314.60 (c), Taylor Pharmaceuticals certifies that a true copy of this Facsimile Amendment to ANDA 75-086 for Diltiazem Hydrochloride Injection, 5 mg/mL, has been provided to the FDA Chicago

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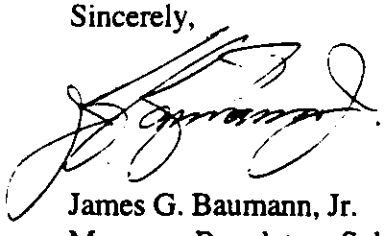
District Office. A copy of this certification with an original signature is provided with this amendment as **Attachment N.**

Should additional information be required regarding this amendment, please feel free to contact me at (217) 423-9715 or FAX (217) 428-8514.

Sincerely,



James G. Baumann, Jr.
Manager, Regulatory Submissions

TABLE OF CONTENTS

	Page
SIGNED APPLICATION FORM - 356h	**1**
Copy of the FDA Deficiency Letter (Facsimile), dated October 17, 1997	**2**
Taylor Response (FACSIMILE AMENDMENT) to the Deficiency Letter, dated October 17, 1997	**13**
ATTACHMENTS:	
Attachment A - Revised Master Record "Signature Pages" *(both vial sizes)* indicating Manufacturing site/address of Diltiazem HCl	**27**
Attachment B - Memo to File: Handwritten Changes to Master Record pages	**31**
Attachment C - Revised Stability Protocol *for both* Vial sizes	**34**
Attachment D - Revised Stability Reports *for both* Vial sizes	**36**
Attachment E - Final Report: Product Bubble Point Determination for Diltiazem HCl (7/26/96)	**38**
Attachment F - Corrected Bubble Point pages for Rev. #2 Master Records *(both vial sizes)*	**62**
Attachment G - Legend for Figures in SOP #s 1945 and 1946	**64**
Attachment H - Oven Loading Patterns: Load #9 and Load #7	**66**
Attachment I - Autoclave Load #12 Diagram/Description	**68**
Attachment J - Validation Report for Autoclave Load #11	**70**
Attachment K - Side-by Side Comparisons and Final Container Labeling *(labeling "proofs")*	**119**
Attachment L - Side-by Side Comparisons and Final Carton Labeling *(labeling "proofs")*	**121**
Attachment M - Side-by Side Comparisons and Final Package Insert Labeling *(labeling "proofs")*	**135**
Attachment N - Signed Certification of Field Copy	**146**

Taylor
Pharmaceuticals an Akorn Co.

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May 15, 1997

NDA ORIG AMENDMENT

N/AA

Office of Generic Drugs, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: AMENDMENT TO ANDA 75-086
Diltiazem Hydrochloride Injection, 5 mg/mL
5 mL and 10 mL Vials

Dear Sir/Madam:

In accordance with 21 CFR § 314.96 (a)(1), and by reference § 314.60 (a), Taylor Pharmaceuticals (an Akorn Company), a manufacturer, marketer, and distributor of ophthalmic and injectable drug products hereby submits this Amendment to our Abbreviated New Drug Application for Diltiazem Hydrochloride Injection, 5 mg/mL, an injectable drug intended for use in adult patients for the temporary control of rapid ventricular rate in atrial fibrillation or atrial flutter and for the rapid conversion of paroxysmal supraventricular tachycardias (PSVT) in sinus rhythm. The reference listed drug (RLD) is Cardizem® Injectable, the subject of NDA 20-027, which is held by Marion Merrell Dow and was approved on October 24, 1991.

This amendment revises existing information and provides the following additional information not previously submitted with the original application, dated February 28, 1997:

- A revised copy (**Attachment A**) of Taylor Pharmaceuticals "SOP RD 113", entitled "Assay of Diltiazem Hydrochloride in Diltiazem Hydrochloride Injection 0.5%" (ref. Vol. 3, Section XVI Analytical Methods, page 1623 of the original ANDA);

- A revised copy (**Attachment B**) of
  " Strength and Purity - Diltiazem Hydrochloride Injection"
  (ref. Vol. 3, Section XVI Analytical Methods, page 1620 of the original ANDA);

MAY 16 1997

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- A copy (**Attachment D**) of the Pall Report #6487 for their - Validation of microbial retention - for Diltiazem Hydrochloride Injection (ref. Vol. 1, Section XI Manufacturing and Processing (extractable substances report), page 445 of the original ANDA); and

- A copy (**Attachment E**) of the Pall Report #6489 for their Extractables report for the for Diltiazem Hydrochloride Injection (ref. Vol. 1, Section XI Manufacturing and Processing (extractable substances report), page 445 of the original ANDA).

Taylor is filing an archival copy consisting of one volume (in blue folder) of this amendment and a technical review copy (in red folder) which is identical to the archival copy. An additional certified field copy (in maroon folder) was sent to the Chicago District Office.

In accordance with 21 CFR § 314.96 (b), and by reference 314.60 (c), Taylor Pharmaceuticals certifies that a true copy of this Amendment to ANDA 75-086 for Diltiazem Hydrochloride Injection, 5 mg/mL, has been provided to the FDA Chicago District Office. A copy of this certification with an original signature is provided with this amendment as **Attachment F.**

Should additional information be required regarding this amendment, please feel free to contact me at (217) 423-9715 or FAX (217) 428-8514.

Sincerely,

James G. Baumann, Jr.
Manager, Regulatory Submissions

ANDA 75-086

Taylor Pharmaceuticals
Attention: James G. Baumann
P.O. Box 1220
Decatur, IL 62525

APR 22 1997

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Diltiazem Hydrochloride Injection, 5 mg/mL
(5 mL and 10 mL vials)

DATE OF APPLICATION: February 28, 1997

DATE OF RECEIPT: March 4, 1997

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Tim Ames
Project Manager
(301) 594-0305

Sincerely yours,

/S/

Jerry Phillips 4/22/97
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Taylor Pharmaceuticals *an Akorn Co.*

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505(j)(2)(A)(ok)
Marie H. Weikel
4/8/97
4/15/97

February 28, 1997

RECEIVED

MAR 04 1997

GENERIC DRUGS

Office of Generic Drugs, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Labeling received 3/27/97 drafted 5/22/97 AVS

RE: ABBREVIATED NEW DRUG APPLICATION
Diltiazem Hydrochloride Injection, 5 mg/mL
5 mL and 10 mL Vials

Dear Sir/Madam:

In accordance with 21 CFR § 314.92 (a)(1), Taylor Pharmaceuticals (an Akorn Company), a manufacturer, marketer, and distributor of ophthalmic and injectable drug products hereby submits this Abbreviated New Drug Application for Diltiazem Hydrochloride Injection, 5 mg/mL, 5 mL and 10 mL vials, an injectable drug intended for use in adult patients for the temporary control of rapid ventricular rate in atrial fibrillation or atrial flutter and for the rapid conversion of paroxysmal supraventricular tachycardias (PSVT) in sinus rhythm. The reference listed drug (RLD) is Cardizem® Injectable, the subject of NDA 20-027, which is held by Marion Merrell Dow and was approved on October 24, 1991. The suitability of the ANDA is documented in the submission.

Akorn, Inc. would like to inform OGD about the following changes in its manufacturing operations: (a) The manufacturing subsidiary has been renamed Taylor Pharmaceuticals, which was previously known as Akorn Manufacturing, Inc., as of August 21, 1996, and (b) Akorn acquired Pasadena Research Laboratories (PRL) of San Clemente, CA during the first half of 1996 and, consequently, some of the documents in this ANDA (e.g., batch records, authorization to reference DMFs) will indicate the name "Pasadena Research Laboratories," or "PRL" since the preparation and use of those documents predate the acquisition.

Taylor Pharmaceuticals would like to clarify that the finished drug product is manufactured for Taylor by located at Information concerning the handling and testing of the raw materials used by to manufacture the drug product, including certificates of analysis, specifications, test methods, and test results of the drug substance used to manufacture the development and scale-up (commercial) batches are included elsewhere in this application **(Section VIII)**. Additionally, the finished product is tested for sterility and SVP particulates by , located at Information concerning s located elsewhere in this application **(Sections IX and X)**. Akorn will be responsible for the

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packaging and labeling of the finished drug product at its manufacturing facility in Decatur, Illinois. Pertinent information concerning these operations can be found in **Section XIII** of this application.

This ANDA is contained in four (4) volumes, and is organized in the manner recommended by the Office of Generic Drugs in its Policy & Procedure Guide 30-91. **At this time, Taylor Pharmaceuticals requests approval for Diltiazem Hydrochloride Injection, 5 mg/mL, (5 mL and 10 mL vial), manufactured according to the attached documentation, using diltiazem hydrochloride manufactured by and components manufactured by . An expiration dating period of twenty four (24) months is requested, based on the available three months acceptable stability data from stability batches stored at accelerated stability conditions.**

This submission contains sterility assurance data. In support of this application, we are providing documentation for the sterilization process validation for diltiazem hydrochloride injection as part of this submission (the aseptic validation package) in **Volume 4**. This documentation is organized according to the directives presented in the "Guidance for Industry for the Submission of Documentation for Sterilization Process Validation in Applications for Human and Verterinary Drug Products" (November, 1994).

Taylor is filing an archival copy (in blue folders) of the ANDA, a technical review copy (in red folders), and a field copy sent to the FDA Chicago District Office (in maroon folders). The technical review copy and the field copies are identical to the archival copy and a certification attesting to this is provided with the field copy. Two extra copies of the validation packages for the assay of the active ingredient in the finished dosage form are provided as separately bound and designated volumes. Four copies of the draft labeling are included in all copies of this ANDA.

In accordance with 21 CFR § 314.94 (d)(5), Taylor Pharmaceuticals certifies that a true copy of this Abbreviated New Drug Application for Diltiazem Hydrochloride Injection, 5 mg/mL, 5 mL and 10 mL vials, has been provided to the FDA Chicago District Office. A copy of this certification with an original signature is provided with this application.

Should you have additional questions or if more information is needed, please do not hesitate to contact Laura Shotton, Regulatory Affairs Specialist, or me at (217) 423-9715, or FAX (217) 428-8514.

Sincerely,

James G. Baumann, Jr.
Manager, Regulatory Submissions